

REMARKS

Applicants thank the Examiner for the thorough consideration given the present application.

Claims 1-2, 4, 9-27, 29 and 31 are pending. Claims 1 and 4 are amended. Claims 5-8 and 30 are currently cancelled. No new matter is added. For instance, amended claim 1 finds support in page 7, lines 9-18 of the present specification and Fig. 2a. Also, amended claim 4 is clarified according to the Examiner's suggestion. Thus, no new matter has been added.

Withdrawn claims 9-25 directed to a method for preparing a biochip of claim 1 have not been cancelled. Applicants respectfully request that these method claims be rejoined upon allowance of claim 1.

The Examiner is respectfully requested to reconsider the pending application, as amended.

Objection to Claim 4

Regarding the objection to dependent claim 4, this claim is amended to match the preamble of claim 1. Thus, the objection is rendered moot.

Issues under 35 U.S.C. §§102(b) and 103(a)

The following rejections are pending:

1) Claims 5-6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim et al. (Biotechnology and Bioengineering, vol. 73, pages 331-337 (5 June 2001)).

2) Claims 1-2, 26-27 and 30 are rejected under 35 U.S.C. 103(a) as being obvious over Kim in view of Simon et al. (USP 5,569,607).

3) Claim 4 is rejected under 35 U.S.C. 103(a) as being obvious over Kim in view of Simon and further in view of Malhorta (USP 5,624,743).

4) Claim 7 is rejected under 35 U.S.C. 103(a) as being obvious Kim in view of Simon.

5) Claim 29 is rejected under 35 U.S.C. 103(a) as being obvious over Kim in view of Simon, and further in view of Croxson (USP 5,108,891).

6) Claims 1-2, 26-27 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim in view of Simon and further in view of Maracas (USP 5,725,788).

7) Claim 4 is rejected under 35 U.S.C. 103(a) as being obvious over Kim in view of Simon and in view of Maracas and further in view of Malhorta.

8) Claim 29 is rejected under 35 U.S.C. 103(a) as being obvious over Kim in view of Simon and in view of Maracas and further in view of Croxson.

9) Claim 30 is rejected under 35 U.S.C. 103(a) as being obvious over Kim in view of Simon and in view of Maracas and further in view of Fang et al (US Publication No. US 2002/0094544).

Applicants respectfully traverse these rejections.

While not conceding to the Examiner's rejections, in an effort to expedite prosecution only, independent claim 1 is amended to further emphasize the distinctions between the present invention and the cited art.

Claim 1 of the present invention is directed to a biochip, comprising: a chip substrate; circular porous gel spots mounted and immobilized on said chip substrate, wherein said gel spots have spherical shape of three-dimensional structure and pores therein; and biomaterials entrapped in said pores of said gel spots and encapsulated by said gel spots, and said biomaterials have a free orientation without being covalently bound to the gel, wherein said gel spots are glassy gel formed by the gelation of a sol mixture containing: biomaterials; at least one silicate monomer selected from the group consisting of tetramethyl orthosilicate (TMOS), tetraethyl orthosilicate (TEOS), methyltrimethoxysilane (MTMS), ethyltriethoxysilane (ETEOS), trimethoxysilane (TMS), and 3-aminopropyltrimethoxysilicate (APTMS); and at least one additive selected from the group consisting of polyglyceryl silicate (PGS), 3-glycidoxypropyltrimethoxysilane (GPTMS), (N-triethoxysilylpropyl)-O-polyethylene oxide urethane (PEOU), glycerol and polyethylene glycol (PEG), wherein said chip substrate is selected from the group consisting of polymethyl methacrylic acid (PMMA), polycarbonate (PC) and cyclic olefin copolymers (COC) and coated with a coating agent selected from the group consisting of polyvinyl acetate (PVAc) having a molecular weight in the range of 800 to 200,000, poly(vinyl butyral-co-vinylalcohol-co-vinyl acetate) having a molecular weight in the range of 70,000 to 120,000, poly(methyl methacrylate-co-methacrylic acid) having a molecular weight of 10,000 or more, poly(methyl vinyl ether-maleic anhydride) having a molecular weight of 200,000 or more, poly(methyl vinyl ether-maleic anhydride) having a molecular weight of 1,000,000 or more, poly(methyl acrylate) having a molecular weight of 10,000 or more, 3-glycidoxypropyltrimethoxysilane (GPTMS), dissolved in solvent(s) selected from the group consisting of methylene chloride, tetrahydrofuran, ethanol, methanol, butanol, methyl ethyl

ketone, acetone, isopropyl alcohol, ethyl acetate, methyl isobutyl ketone, and di-acetone alcohol, and wherein up to 1000 spots/cm² are integrated on the chip substrate.

In particular, amended claim 1 of the present application has the following features:

- (i) Morphology of the spots: the gel spots are circular, porous, and spherical shape and up to 1000 spots/cm² integrated on the chip substrate;
- (ii) Sol mixture recited in claim 1
- (iii) Type of chip substrate: a plastic chip substrate, such as PMMA, PC, COC, etc;
- (iv) Treatment of the chip substrate: the chip substrate is coated with a specific coating agent which is a sol mixture containing biomaterials. This sol mixture containing biomaterials can be integrated in a spot form on the chip substrate. In addition, glassy gels containing silicate can be immobilized to the substrate; and
- (v) Mobility of biomaterials: the biomaterials are not immobilized or covalently bound to the gel matrix to thereby have a free orientation.

By way of the present invention, the biochip has silicate gel spots formed by Sol-Gel transition. Specifically, the gel spots can be integrated in an amount of up to 1000 spots/cm² as recited in claim 1.

Until now, since there have been no technologies which can adhere a sol-gel matrix containing biomaterials in the shape of spots on a chip substrate, there has also been no biochip comprising the sol-gel matrix integrated in a spot form. See paragraph [0016] of the US publication of the present application.

In this connection, the Kim reference discloses technologies for patterning a protein by previously mixing the protein with a sol using various mild conditions such as neutral pH.

However, there exist problems such as the sol-gel process rapidly progressing to gel at neutral pH, cracks occurring or the gel turning opaque, according to additives (see page 4, lines 1-4 of the present specification).

However, by developing a chip substrate surface treatment technology, the present invention can provide a biochip produced using the sol-gel reaction on a chip substrate for the first time.

In other words, 1) a sol mixture containing a biomaterial and a silicate monomer can be integrated in a spot form on a chip substrate, 2) a sol-gel reaction to gel the sol mixture can occur on a chip substrate, and 3) a sol-gel matrix can be immobilized on a chip substrate by the chip substrate surface treatment technology according to the present invention.

Since the silicate gel spots are not deformed by any outside pressure, a three-dimensional structure can be maintained. Thus, it is possible to produce a chip with improved sensitivity and to exert superior storage properties. In addition, the glassy gel can be easily manufactured by Sol-Gel transition.

More specifically, EXAMPLE 3 (see paragraphs page 14, line 1-page 16, line 4 of the present specification) shows superior effects that the silicate monomer and additives contributed to the formation of spots with excellent three-dimensional structure. Further, Experiments 3-5 (see page 17, line 23-page 18, line 4 of the present specification) show that the spots formed by the gelation according to the present invention are transparent, have no crack, and stable for more than six months.

Also, since many proteins can be stabilized by biocompatible additive(s) in a silicate structure which is a basic component of the sol-gel reaction, their activities can be remarkably improved.

By way of the claimed features, the biochip according to the present invention has superior properties in view of reactivity and sensitivity, as evidenced by Experiments 1-5 of the present specification.

However, the Kim reference (which is the primary reference utilized in all rejections) fails to disclose or suggest the claimed features. Rather, Kim is interested mainly in encapsulation within microchanneled sol-gel networks and thus is focused on the structure or size of pores suitable for encapsulating biomaterials. Specifically, Kim does not disclose or suggest the claimed features that the biomaterials are entrapped in pores of gel spots on a chip substrate, the gel spots are circular and spherical shape of three-dimensional structure and the sol mixture contains biomaterials, at least one specific silicate monomer and at least one specific additive.

Accordingly, the present invention is neither anticipated by nor rendered obvious over the Kim reference.

Further, the deficiencies of the Kim reference cannot be remedied by the secondary references including Simon, Malhorta, Croxon, Maracas and Fang because they also fail to disclose or suggest the claimed features of the biochip. Therefore, the cited references alone or in combination neither suggest nor disclose the presently claimed biochip.

As the MPEP directs, all the claim limitations must be taught or suggested by the prior art to establish a *prima facie* case of anticipation or obviousness. See MPEP §§ 2131 and 2143.03.

In view of the fact that the cited references fail to teach or fairly suggest the claimed features, a *prima facie* case of anticipation or obviousness cannot be said to exist.

For the reasons above, since amended independent claim 1 of the present application is believed to overcome the 35 USC §§ 102(b) and 103(a) rejections, the claims dependent therefrom are also believed to address the same rejections. Therefore, the Examiner is respectfully requested to withdraw these rejections.

In view of the above remarks, Applicants believe the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Craig A. McRobbie Reg. No. 42,874 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated:

Respectfully submitted,

By 

Craig A. McRobbie
Registration No.: 42,874
BIRCH, STEWART, KOLASCH & BIRCH, LLP
8110 Gatehouse Road
Suite 100 East
P.O. Box 747
Falls Church, Virginia 22040-0747
(703) 205-8000
Attorney for Applicants